

Investigation of the Contribution of Different Antiseptic Solutions to Clinical Recovery in Uroretropropulsion Technique in Cats

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ABSTRACT

The aim of this study was to report the contribution of different antiseptics to clinical improvement during intravesical lavage in cats with urethral obstruction problems. Urethral obstruction (UO) is a problem mostly encountered in male cats, requiring urgent intervention with a high success rate in the inferior urinary system. A total of 42 cats of different breeds and ages were evaluated, and the first medical treatment was applied, but no urine output was detected. All cases were randomly divided into 3 different groups and one-time intravesical lavage was performed with different fluids: GI (0.9% saline), GII (Dimethyl sulphoxide) and GIII (lugol's solution). The controls performed on the 7th, 14th, and 30th days of the study showed similar results in all cases, and no statistically significant difference was determined. As a result, it was concluded that lugol's solution can be used as a new alternative to DMSO antiseptic, which is the only agent approved for treatment by the US Food and Drug Administration, when performing intravesical lavage in cats with urethral obstruction.

INTRODUCTION

Urethral obstruction (UO) in cats is a mostly encountered lower urinary system problem that requires urgent intervention and has a high success rate when treated. However, recurrence rates vary between 22-57% and are mostly observed in male cats (Kim et al., 2011; Eisenberg et al., 2013; Reineke et al., 2017). The underlying causes of UO often cannot be determined, dietary factors such as urine pH, obesity, stress and other environmental factors, urethral plugs (proteinaceous debris in which crystals can become trapped), and urethral spasm are known to be involved. Feline idiopathic cystitis (FIC), also known as 'stress cystitis', causes urethral obstruction in 65-90% of cases (Breheny et al., 2022a).

Clinical symptoms of UO often include stranguria, pollakiuria, periuria (inappropriate urination), haematuria, lethargy, vomiting, abdominal pain symptoms and painful

vocalisations. Urethral obstruction is a serious urinary tract problem that can lead to postrenal azotemia and severe metabolic abnormalities (Lee and Drobatz, 2006; Cooper et al., 2019). Emergency treatment of cats with UO includes anesthesia, retrograde urethral lavage to ensure clearance, compositions of fluid and electrolyte residues, permanent urethralization connected to a sterile closed collection system for a period of 24 to 48 hours, and the use of non-steroidal agents and α -1 adrenergic receptor antagonist systems (Segev et al., 2011; Hetrick and Davidow, 2013). However, it should be noted that indwelling urinary catheter placement in cats with UO has been shown to increase the risk of urinary tract infection due to bacterial biofilms colonising the catheter surface (Delcaru et al., 2016). Several agents are used during intravesical lavage application, including dimethyl sulphoxide (DMSO), hyaluronic acid, heparin, Bacillus

Calmette-Guerin, pentosan polysulphate sodium, and resinferatoxin (Fall et al., 2008; Dasgupta and Tincello, 2009). DMSO is the most widely used antiseptic and the only agent approved for intravesical treatment by the US Food and Drug Administration in 1978 (Hanno et al., 2010). Lugol's solution, also known as Lugol's iodine, has been used as an antiseptic in different medical care in cats since the 19th century. It was described by French physician JGA Lugol in 1829 and consists of 85 mL of distilled water with 5 g of iodine (I₂) and 10 g of iodide (KI). Its antimicrobial effect is based on the degree to which free iodine remains bound to cell wall, oxidation and supplementation of the microbial content with free iodine (Grønseth et al., 2023).

The main aim of this study is to determine the clinical recurrence rates of 42 male cats with idiopathic UO of different breeds and ages at 7, 14 and 30 days after 3.5Fr indwelling catheterisation and one-time lavage with different antiseptics. Our hypothesis is that the use of Lugol's solution in one-time retrograde intravesical lavage will contribute to the clinical improvement in cats with UO undergoing indwelling catheterisation.

MATERIALS AND METHODS

This study is not subject to HADYK permission in accordance with Article 8 (k) of the "Regulation on Working Procedures and Principles of Animal Experiments Ethics Committees".

The material of the study consisted of 42 male cats that presented to Dicle University, Faculty of Veterinary Medicine, Department of Surgery with the complaint of inability to urinate and were previously treated medically. In all cases, the first empirical treatment was applied but no urine output was detected. Male cats suspected of having feline idiopathic cystitis (FIC) were prospectively included in the study. The diagnosis of urethral obstruction was based on initial physical examination (hard, painful, swollen bladder) and a history of signs of feline lower urinary tract disease (pollakiuria, haematuria, stranguria and vocalisation). Exclusion criteria included cats with UO caused by other underlying disease rather than FIC, such as urinary tract infection, radiographic cystic calculi and neoplasia.

The anesthesia protocol applied to all groups during the application is; Midazolam + butorphanol + ketamine as 0.3 + 0.3 + 5 mg/kg IM determined.

All cats in the group underwent one-time intravesical lavage by applying an intravesical catheter after anesthesia (Fig 1). Medical empiric treatment in cats was continued for 5 more days.

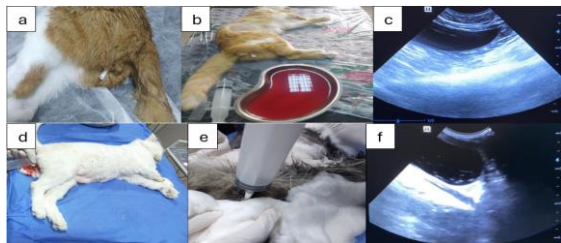


Figure 1. Images of some cases during the procedures performed

- a) Intravesical catheter application and fixation
- b) Haematuria in the tub as a result of intravesical ejaculation
- c) Ultrasound view of the intravesical catheter
- d) Intravesical catheter application and haematuria
- e) Intravesical lavage application
- f) Appearance of the sac during intravesical lavage

In the diagnostic examination; anamnesis, clinical examination, haematology, radiography, and ultrasonography were performed appropriately in each cat. The urinary catheter was removed at the 24th hour in order to relieve the patients from the stress factor, and the issues to be considered during the surveillance (especially ensuring that the patients drink plenty of water, cleaning of wet food and urine containers) were explained to the patients' relatives and they were warned to bring them back for follow-up if the problem persisted.

Follow-up evaluation was performed through clinical evaluation of the animals and telephone interviews with relatives. Data collected include the duration of hospital stay, emergency treatment, post-discharge treatment and time until symptoms reappear, nature of clinical signs (obstruction, other signs of urinary tract disease such as hematuria, pollakiuria, choking, urination in inappropriate places, and pain) was taking. Glasgow Feline Composite Measure Pain Scale was used in all cases and repeated analgesics were administered if necessary.

RESULTS

In this study, the average age range of 14 cats in GI was 28±5 months and 7 Scottish folds, 2 Iranian, 3 tabby, 2 crossbred, the average age range of 14 cats in GII was 28±8 months and 6 Scottish Folds, 1 Iranian, 4 tabby, 3 crossbred, the average age range of 14 cats in GIII was 28±7 months and 6 Scottish Folds, 2 Iranian, 3 tabby, 3 crossbred.

Since empirical treatment (amoxicillin+cluvanic acid, meloxicam, oxybutynin hydrochloride) was previously applied in all cases of this study, vesical bacterial load could not be defined in all included cases. Thus, differences between of groups in terms of clinical recovery levels in terms of 0.9% saline and different antiseptics (DMSO, Lugol's solution) of the lavage to be applied during intravesical catheter insertion were investigated. No complications were encountered during or after anaesthetic administration in all cases. The dose of anaesthesia administered was adequate and no maintenance dose was needed until the end of the procedure. All cases woke up after the procedure without complications. In terms of pain management, it was determined that all cases needed analgesic at 24 hours according to the results of Glasgow Feline Composite Measure Pain Scale. No significant difference was found between the groups in terms of pain.

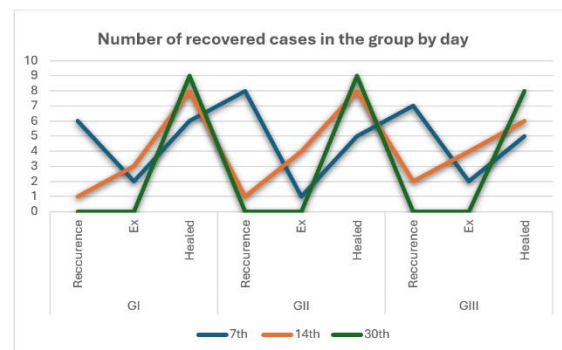


Figure 2. Survival rates by groups and recurrence numbers by days are given

The recovery, recurrence and ex rates according to the groups and the days of recovery are shown in the fig 2.

There was not statistically significant difference with antiseptic fluids used during lavage between the groups.

According to the results of the study, it was determined that the cats that died were caused by Iranian and Scottish Fold cats. It was determined that the recovery rates of tabby breed cats were better and the recurrence rates were lower. In all cases, it was aimed to maintain indwelling catheterisation for 24 hours, but the tabby breeds were uncomfortable with the catheter and removed it in the 9th hour with the help of tongue and teeth, although an Elizabethan collar was worn. No wound or infection was detected at the suture site. In all cases, the diet and toilet cleaning applied in the postoperative period were followed, 2 cases in GI and GII were reported to be stray animals and were released back to their place in the street since no complication occurred until the 18th day and they were followed up in the street until the 30th day. No signs of allergic reaction were found in any of the 14 cases as a result of lavage using Lugol's solution. The rate of haematuria was quite high in all groups of the study. Recurrence and ex in all cases; 6 of 14 cases developed recurrence and 2 cases died until the 7th day in GI. In the continuation of the follow-up until the 14th day, the condition of 2 of the 6 cases with recurrence improved, while the recurrence of 1 case continued and 3 cases died. On the 30th day of the study, a total of 5 cases died and no clinical symptom was found in a total of 9 cases. Thus, the survival rate of GI on the 30th day was determined as 64%. When we evaluated this situation for GII; recurrence developed in 8 of 14 cases and died in 1 of 14 cases until the 7th day. In the continuation of the follow-up until the 14th day, the condition of 3 of the 8 cases who had previously developed recurrence improved, while the recurrence of 1 case continued and 4 cases died. On the 30th day of the study, a total of 5 cases exited and no clinical symptom was found in a total of 9 cases. In this case, the survival rate of GII on the 30th day was determined as 64%. In GIII in which Lugol's solution was used, 7 of 14 cases developed recurrence and 2 cases died until the 7th day. In the continuation of the follow-up, the condition of 1 of the 7 cases which developed recurrence until the 14th day improved, while the recurrence of 2 cases continued and 4 cases died. On the 30th day of the study, a total of 6 cases died and no clinical symptom was found in a total of 8 cases. In this case, the survival rate of GIII on the 30th day was determined as 57%. The rates of recurrence, ex and recovered cases at day 7 were determined as GI 42-14-42%, GII 57-7-35% and GIII 50-14-35%, respectively, and at day 14 as GI 7-21-57%, GII 7-28-57% and GIII 14-28-42%.

DISCUSSION AND CONCLUSION

The aim of this study was to examine the clinical differences between the use of different antiseptics (DMSO, Lugol's solution) and 0.9% saline in the lavage performed during indwelling catheterisation in addition to empirical treatment in cats with UO.

Studies have shown that UO has different causes, 60% have urethral obstruction, 20% have urethral calculi, <5% have stricture or neoplasia. In the remainder, there is no clear evidence of physical obstruction and the disease is supported by previous aetiological studies (Gerber et al., 2008).

In the present study, cats with urethral plugs, which are encountered with a high rate of 60%, were selected. Thus, it was aimed to prevent intravesical infections that may occur with catheter application with the help of lavage

performed during indwelling catheterisation in urethral plugs. Cooper et al., (2019) reported that 13% of cats without intravesical lavage developed bacteriuria within 24 hours after urinary catheterisation. However, urine cultures were obtained through the catheter and therefore it is thought that the biofilm sample may have been taken rather than the actual colonisation in the lower urinary tract. Although one of the disadvantages of the present study was that urine culture results could not be obtained, they were not obtained because culture tests did not give reliable results since empirical treatment was initiated in all cases and all cases were cats presenting with persistent UO. However, since it was aimed to investigate the clinical efficacy of permanent catheterisation and lavage applications in addition to empirical treatment, urine culture tests were ignored and clinical improvements were evaluated.

It is known that clinical symptoms observed in the studies depend on the duration and intensity of the obstructive event, and haematuria, pollakiuria and stranguria are commonly reported clinical symptoms (Ferreira, 2013; Breheny et al., 2022a). In our study, similar results were encountered and it was determined that all cases had similar clinical symptoms and different antiseptics used during lavage did not make any difference in clinical recovery. The small number of cases in the present study necessitates the need for further studies on this subject.

The intravesical administration of DMSO used in the current study one of the primary treatment for IC/PBS patients and an FDA-approved treatment option for IC/PBS. This therapeutic modality has proven to be feasible and effective in the treatment of this painful urinary condition (Kim et al., 2011). Considering this situation, DMSO used in the present study has been used in many previous studies and the decrease observed in NGF, MCP-1 and IL-6 mRNAs in DMSO treated bladders may reveal the inhibitory effect of DMSO on the abnormal activation of sensory neurons, urothelial cells, mast cells and detrusor muscle cells. Therefore, the general anti-inflammatory effects of DMSO are thought to help inhibition of many inflammatory cell types in infected bladders. However, no difference was found between saline, Lugol's solution and DMSO groups used in the present study. The reason for this is thought to be that all of the treated cats were treated with antibiotics and NSAID agents in their empirical treatments. In addition, in an experimental mouse model by Soler et al., (2008), intravesical DMSO also showed a similar protamine sulphate-induced reduction of hyaluronic acid levels in urine, suggesting that it may regenerate the damaged glycosaminoglycan (GAG) layer (Soler et al., 2008).

However, the fact that there is no clinical difference in different fluids used during intravesical lavage does not support the opinion of Soler et al., (2008), in addition, there is various hypotheses regarding mechanism of action topical application in iodine solution. Several studies have shown that iodide is an anti-inflammatory effect resulting from its ability to down-regulate free oxygen radicals produced by polymorphonuclear cell activation. Another hypothesis for its anti-microbial role is based on the participation of iodide in halogenation reactions mediated by oxidase, which is essential for phagocyte function. Iodine solution used in topical treatment browns the skin and evaporates rapidly. It is argued that one application loses 50% of the free iodine in two hours, 80% in two days 88% evaporates on third day. Lugol's solution has proven

useful in inflammatory, infectious pathologies, immune-mediated therapies (Taranu et al., 2018). Likewise, the fact that intravesical lavage showed similar results to DMSO antiseptic in the present study and no allergic effect was encountered in clinical use, we believe that intravesical lavage may be useful in the use of intravesical lavage in cats and may be an alternative to DMSO antiseptic.

In all cases, empirical treatment and fluid therapy were generally provided with similar protocols. Fluid administration is needed to increase urine production and clear urine components. Higher fluid volumes may theoretically reduce the risk of UO recurrence. However, a recent study found no relationship between UO and the total volume of fluid administered during hospitalization or the duration of fluid administration after permanent removal of the urethral catheter. To our knowledge, there are no studies evaluating the effect of a single fluid dose in cats with UO; However, the 1996 study by Osborne et al. 1996 suggest that this type of treatment is not effective enough to show any benefit in reducing the clinical signs associated with feline idiopathic cystitis (Osborne et al., 1996).

In the present study, since classical empirical treatment was applied to all cases, similar results were found with the studies that there was no clinical relationship between fluid therapy and recurrence rate in UO cats.

This is because the cat's urethra is known to consist of smooth muscle only along the proximal 28% to 37% of its length, and the remainder of the urethral musculature is known to consist of non-relaxing muscle with α -1, so the second dose was not used other than spasmolytic agents used in empirical therapy due to adrenoceptor blockade. Lulich et al. 2013 argue that the pharmacological activity and potential smooth muscle relaxant effect of prazosin make urethral muscle relaxation an ineffective management strategy in cats with UO (Lulich and Osborne, 2013). In the current study, Breheny et al., (2022b) argue that the likelihood of dehydration and re-occlusion in the post-catheterisation period is most likely to occur in the week following the first episode and the likelihood of feeding is low. He argues that NSAIDs should be avoided as renal perfusion is not guaranteed.

In our study, it was observed that a large proportion of recurrences occurred in the first week in all groups. However, NSAIDs were used in all cases due to the high pain scores used in our study. H-2 blockers were used in all cases because of the second dose used due to the presence of pain in the cases.

In the present study, there was no statistically significant difference between the recurrence, ex and recovery rates on the 7th, 14th, 30th days. The similarity of all results due to the similarities in markers such as gender and age of the cases in the group distribution, in fact, it was concluded that intravesical lavage contributes to clinical recovery when used for the removal of UO rather than the fluid used during intravesical lavage. It was concluded that lugol solution can be used as an alternative to DMSO used as an antiseptic for intravesical lavage in addition to the medical treatment of UO which is frequently encountered in cats.

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Ethical Declaration

This study is not subject to HADYEK permission in accordance with Article 8 (k) of the "Regulation on Working Procedures and Principles of Animal Experiments Ethics Committees". (In this case, the "Ethics Statement Form" or "Informed Consent Form" must be filled in, signed by all authors and uploaded to the system.)

Conflict of Interest

The authors declare that they have no competing interests.

Authorship contributions

Idea / Concept: NS, US, Supervision / Consultancy: NS, US, Data Collection and / or Processing: NS, Analysis and / or Interpretation: NS, US, Writing the Article: NS, US, Critical Review: NS, US.

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